PNEUMOCOCCAL DISEASE

IN THIS CHAPTER

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1. Introduction

As part of the National Action Plan to Combat Antimicrobial Resistance, the Centers for Disease Control and Prevention (CDC) has the responsibility to coordinate a national surveillance approach to monitoring drug-resistant infections. (Please visit, http://www.cdc.gov/drugresistance/actionplan/2001report/index.htm)
Additionally, the Council of State and Territorial Epidemiologists (CSTE) has passed resolutions recommending that states adopt mandatory reporting of invasive infections caused by drug-resistant *Streptococcus pneumoniae*. Active, population-based surveillance based on laboratory confirmed invasive disease may be considered the most accurate method of assessing the burden of disease and for monitoring trends, but because it is labor-intensive and costly this method is an impractical option for most state health departments to use. However, as state and local health departments launch campaigns for vaccine promotion and appropriate antibiotic use, the need to identify feasible but reliable surveillance systems for wide scale implementation is urgent.

CDC has developed this manual for state or local health departments carrying out surveillance of *S. pneumoniae* with the collaboration of local health partners. This document describes available options for the surveillance of *S. pneumoniae.* Its purpose is to assist health departments' personnel identify an efficient and effective surveillance system that meets specific surveillance goals. It contains guidance on planning and

implementing surveillance methods that are accurate, timely, and nationally comparable, along with practical tools such as forms for laboratory surveys and data collection.

This manual will guide staff through a menu of different surveillance methods and outlines each method's required resources, advantages and disadvantages, data collection requirements, and implementation. Additionally, this manual addresses other key considerations such as laboratory issues, control measures for pneumococcal disease and antibiotic resistance, and electronic reporting.

2. Why Monitor for Drug-Resistant *Streptococcus pneumoniae*?

S. pneumoniae infections are among the leading causes worldwide of illness and death for young children, persons with underlying debilitating medical conditions, and the elderly. Pneumococcal infections range in clinical manifestation from otitis media and bacteremia to pneumonia and meningitis. Pneumococcus is the most commonly identified cause of bacterial pneumonia. Since the widespread use of vaccines against *Haemophilus influenzae* type b, pneumococcus has become the most common cause of bacterial meningitis in the United States.(1) CDC's Active Bacterial Core Surveillance (ABCs) has tracked invasive pneumococcal disease (IPD) in select regions of the United States since 1994. ABCs data suggest that individuals < 2 years of age and 65 years and older account for over half of all cases. (2)

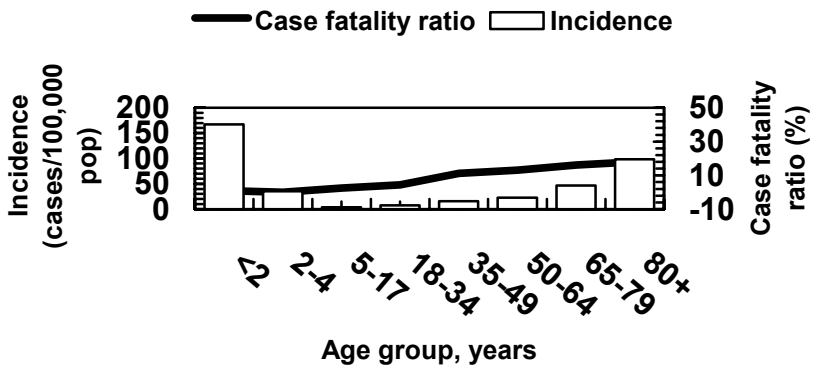
Pneumococcal Infections in the United States, 1999

Type of Infection	# cases/ year
Meningitis	3,000
Bloodstream infection	63,000
Pneumonia (hospitalized)	125,000
Ear Infections (AOM)	6,000,000

source: CDC Active Bacterial Core Surveillance (ABCs)

Approximately 10% of all patients with invasive pneumococcal disease die of their illness, but case-fatality rates are higher for the elderly and patients with certain underlying illnesses. (3) Acute otitis media and other upper respiratory tract infections do not commonly progress to invasive disease but they do contribute significantly to the burden and cost of healthcare. (4)

Incidence and Case Fatality Ratio of Invasive Pneumococcal Disease by Age Group
ABCs 1998

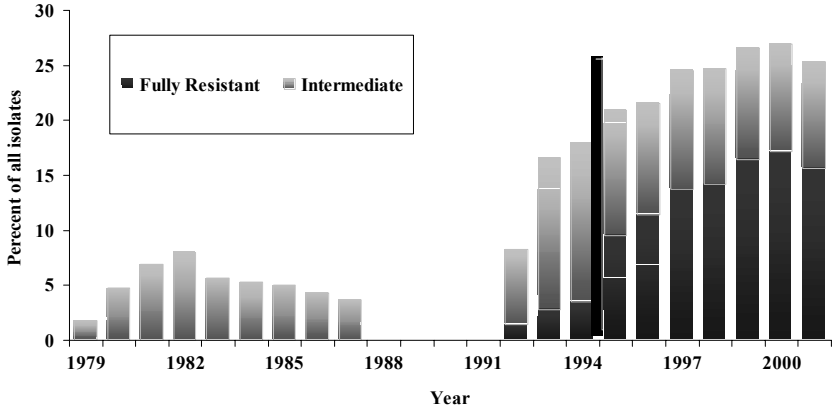


Source: 2000 CDC Active Bacterial Core Surveillance (ABCs), Emerging Infections Program

3. Antimicrobial Resistance to Common Drugs

Penicillin has traditionally been an effective treatment for pneumococcal infections. Reports of DRSP infection (including strains resistant to penicillin, extended spectrum cephalosporins and other drugs) have been increasing in the United States since the 1980's. (5) In some areas of the United States, over 30% of isolates are not susceptible to penicillin.

Penicillin Resistance in *S. pneumoniae*
United States 1979-2001



1979-1994: CDC Sentinel Surveillance Network
1995-2001: CDC Active Bacterial Core Surveillance (ABCS) System
Emerging Infections Program

With the widespread use of antimicrobials, the prevalence of resistance to each new drug class has increased. (6) Recent trends have shown an increasing prevalence of *S. pneumoniae* with intermediate or high-level resistance to penicillin and other commonly used antibiotics. (7) Many penicillin-resistant strains of *S. pneumoniae* are also resistant to other antimicrobials such as erythromycin, trimethoprim-sulfamethoxazole, and many of the cephalosporins. (8)

The proportion of pneumococcal illnesses caused by drug-resistant *S. pneumoniae* among children may be higher than among adults, and the incidence of drug-resistant infections can change rapidly. (9) Outbreaks due to susceptible *S. pneumoniae* and DRSP have been reported in child-care centers and among residents of long-term care facilities in which pnemococcal vaccine coverage was low. (10,11,12)

4. Clinical Impact of Resistance for Pneumococcal Syndromes

The increasing prevalence DRSP in the US has not only complicated empiric treatment but has led to increased numbers of treatment failures. Treatment failures due to drug resistance have been reported with meningitis and otitis media. The relationship between drug resistance and treatment failures among patients with pneumococcal pneumonia is

less clear. (13) Failures are likely to occur in pneumonia patients with high-level but not intermediate-level resistance. (14)

The emergence of DRSP has made treatment of pneumococcal disease more difficult. Because of a lack of rapid, sensitive, and specific diagnostic tests, therapy for pneumonia and milder illnesses such as otitis media remains empiric. Groups of experts have made recommendations for treating infections commonly caused by pneumococcus, such as otitis media and pneumonia, accounting for the increasing prevalence of DRSP. (15,16) Few communities remain in which resistance is not yet a problem and even in communities with lower rates, resistant infections can occur. Because of the limitations of current diagnostic testing, clinicians may prescribe therapy for infections that is not indicated or is unnecessarily broad. Inappropriate antimicrobial use contributes to the development of DRSP (17). Principles have been developed to encourage appropriate use of antimicrobial agents for adults and children with upper respiratory infections (18).

Consequences of Antimicrobial Resistance

Mortality*: resistant infections are more often fatal*
Morbidity*: prolonged illness, greater chance for resistant organisms to spread to other people*
Cost*: increased costs of care, and newer, more expensive drugs*
Limited solutions*: few new drugs on horizon*

Source: WHO Global Strategy for Containment of Antimicrobial Resistance 2001

5. Surveillance Case Definitions

The following three case definitions are used for national surveillance of pneumococcal disease in the United States. The definition for invasive pneumococcal disease in children less than five years of age was approved by the Council of State and Territorial Epidemiologists (CSTE) in 2000. The definition for Drug-Resistant *S. pneumoniae* (DRSP) Invasive Disease in 1994 was approved by CSTE in 1994. (19,20)

I. Invasive *S. pneumoniae* (Children <5 years*)*

Clinical Description

S. pneumoniae causes many clinical syndromes, depending on the site of infection (e.g. pneumonia, bacteremia, or meningitis).

Laboratory criteria for diagnosis

- Isolation of *S. pneumoniae* from a normally sterile site (e.g. blood, cerebrospinal fluid, or, less commonly, joint, pleural, or pericardial fluid).

Case classification

Confirmed: A clinically compatible case in a child less than 5 years of age caused by laboratory-confirmed culture of *S. pneumoniae* from a normally sterile site.

II. Drug-resistant *S. pneumoniae* (DRSP) Invasive Disease

Clinical Description

S. pneumoniae causes many clinical syndromes, depending on the site of infection (e.g. pneumonia, bacteremia, or meningitis). (21)

Laboratory criteria for diagnosis

- Isolation of *S. pneumoniae* from a normally sterile site (e.g. blood, cerebrospinal fluid, or less commonly, joint, pleural, or pericardial fluid) AND
- "Nonsusceptible" *S. pneumoniae* isolate (i.e., intermediate- or high-level resistance* to at least one antimicrobial agent currently approved for use in treating pneumococcal infection.

  *Resistance defined by National Committee for Clinical Laboratory Standards (NCCLS)-approved methods and NCCLS-approved interpretive minimum inhibitory concentration (MIC) standards (μg/ml) for *S. pneumoniae.* NCCLS recommends that all invasive *S. pneumoniae* isolates found to be "possibly resistant" to beta-lactams by oxacillin screening should undergo further susceptibility testing by using a quantitative MIC method acceptable for penicillin, extended-spectrum cephalosporins, and other drugs as clinically indicated.

Case Classification

Confirmed DRSP case: A clinically-compatible case caused by laboratory-confirmed culture of *S. pneumoniae* identified as "nonsusceptible" according to MIC laboratory criteria listed above.

Probable DRSP case: A clinically compatible case caused by laboratory-confirmed *S. pneumoniae* identified as "nonsusceptible" (i.e., an oxacillin zone size of less than

20mm) when oxacillin screening is the only method of antimicrobial susceptibility testing performed.

Comment: There are a variety of methods with which a laboratory can determine the antimicrobial susceptibility of *S. pneumoniae*, commonly including disk diffusion, testing by agar dilution or broth microdilution, and testing by antimicrobial gradient agar diffusion (Etest® method). When oxacillin disk screening is the only antimicrobial susceptibility method used, the antimicrobial susceptibility profile cannot be definitely determined. Oxacillin screening is highly sensitive for detecting beta-lactam-resistant *S. pneumoniae*; in addition, resistance to non-beta-lactam antibiotics is not detected with this screening method (see "VI. Laboratory testing").

Comment: 2002 NCCLS guidelines recommend using an MIC method immediately, without first using an oxacillin screen, for isolates from patients with life-threatening infections.

III. Invasive Pneumococcal Disease in Children <5 Who Have Received Pneumococcal Conjugate Vaccine.

Cases are limited to children <5 years of age with invasive pneumococcal infections, defined as *S. pneumoniae* isolated from a normally sterile body fluid, who have received at least one dose of PCV7. These cases are not nationally reportable but are part of a voluntary surveillance system for possible vaccine failures. For more information on reporting these cases see http://www.cdc.gov/nip/diseases/pneumo/PCV-survrpts/default.htm.

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